IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Martin BILLGER *et al.*

Title: PROTEIN FORMULATIONS

Appl. No.: 09/674,002

Filing Date: 12/27/2000

Examiner: Ruixiang Li

Art Unit: 1646

PETITION TO MAKE SPECIAL UNDER 37 C.F.R. 1.102 AND M.P.E.P. 708.02 ON THE BASIS THAT APPLICANT IS A SMALL ENTITY AND THE APPLICATION RELATES TO A MAJOR BIOTECHNOLOGICAL ASSET

Mail Stop Petition
Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

Sir:

The Applicant hereby petitions under 37 C.F.R. Section 1.102 and M.P.E.P. Section 708.02 to make this application special because Applicant is a small entity and the subject matter of the above-identified application is a major asset of the Applicant's portfolio.

1. **Statement**

Applicants state that:

(A) small entity status has been established U.S. application 09/674,002;

(B) the subject of U.S. application 09/674,002 is a major asset of the Applicant;

(C) the development of this technology will be significantly impaired if examination of the patent application is delayed. To this end, Applicants respectfully point out that the parathyroid hormone formulation disclosed in the present application is of utmost importance to establishing the assignee's position, commercially and technologically, in the market and scientific community.

Indeed, the assignee's current product candidates include parathyroid hormone-based treatments for bone and mineral disorders, such as osteoporosis and hyperparathyroidism, while the most advanced drug candidates being developed include PREOS(r) (recombinant human parathyroid hormone) for the treatment of osteoporosis. Appended to this paper as Appendices 1 and 2 are copies of literature posted on the assignee's website, which illustrate the importance of the presently claimed parathyroid hormone product to their business interests. Thus, the parathyroid hormone formulation under question is a key counterpart in the assignee's business strategy for developing parathyroid hormone pharmaceuticals. Accordingly, development of this particular product will be significantly impaired if examination of the patent application is delayed.

2. **Fee Under 37 C.F.R. 1.17(h)**

[X] Attached is a Check in the amount of $130.00

[ ] Authorization is hereby made to charge the amount of $130.00

[ ] to Deposit Account No. 19-0741

[ ] To credit card as shown on the attached credit card information authorization form PTO-2038

[X] Charge any additional fees required by this paper or credit any overpayment in the manner authorized above

Respectfully submitted,

Date 28 October 2003 By _____

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market opportunities

NPS Pharmaceuticals is currently developing drugs in several market areas. Below is a discussion of the market opportunities that exist in these areas.

PREOS®

Approximately 10 million American women have advanced osteoporosis and another 18 million women are osteopenic, or approaching osteoporosis, and are at high risk of fractures because of low bone mineral density. A recent study published in the Journal of the American Medical Association demonstrated that nearly one-half of post-menopausal women have undetected low bone mineral density, and women identified with low bone mineral density were at a significantly increased risk of fracture. In addition, 50 percent of women over 50 years of age in the United States will suffer an osteoporosis-related fracture during their lifetime. According to the National Institutes of Health, osteoporosis is responsible for more than 1.5 million fractures annually. The National Osteoporosis Foundation reports that an average of 24 percent of hip fracture patients age 50 and over die within one year after their fracture, and 25 percent of those who were ambulatory before their hip fracture require long-term care afterward. The size of the United States population aged 50 years and over is expected to increase significantly over the next several decades as a result of the aging of the "baby boomer" generation and longer life expectancies. Estimated United States expenditures for osteoporosis and related fractures is $14.0 billion each year.

Current therapies for osteoporosis include supplementing dietary calcium and vitamin D, which may help to slow the rate of bone loss. Other therapies include estrogen replacement therapy in post-menopausal women, bisphosphonates and raloxifene, a selective estrogen receptor modulator. All of these therapies act to prevent further bone loss by inhibiting bone resorption. These therapies have been shown to reduce the incidence of fracture, but they have only a limited positive effect on bone mineral density. For example, Fosamax, a bisphosphonate sold by Merck, showed a reduction in fractures but an increase in bone mineral density of only seven to ten percent over three years. Merck reported sales of Fosamax in 2001 of $1.8 billion.

We believe there exists a significant need for improved therapy that will increase bone mineral density to a greater degree and at a faster rate, thereby reducing the risk of fracture. Parathyroid hormone treatment, such as our product candidate, PREOS, and Lilly's parathyroid hormone-fragment, Forteo, are designed to address this medical need and supplement currently available treatments.

The FDA's Endocronologic and Metabolic Drug Advisory Committee recently recommended Forteo for the treatment of osteoporosis, which we believe further validates the clinical benefit of parathyroid hormone treatment. PREOS is our recombinant parathyroid hormone consisting of all 84 amino acids found in the naturally occurring human parathyroid hormone. Lilly's Forteo is a fragment of the

naturally occurring parathyroid hormone and is only comprised of the first 34 amino acids. Data from Lilly's Phase III clinical trial indicated that, in post-menopausal women with severe osteoporosis, daily injections of Forteo provided statistically significant reductions in fractures and rapid and significant increases in bone mineral density. Because PREOS consists of 84 amino acids found in the naturally occurring human parathyroid hormone, we believe that our Phase III clinical trials will also show efficacy in the treatment of osteoporosis. In addition, studies currently being conducted by us and our academic collaborators are designed to confirm what, if any, therapeutic advantage our full-length human parathyroid hormone may have compared to fragments of parathyroid hormone.

For more information:
drugs in development - PREOS®
therapeutic areas - osteoporosis

cinacalcet HCl

Over 75,000 people in the United States develop new cases of primary hyperparathyroidism each year, and over 500,000 people in the United States are estimated to suffer from the disorder. The current treatment for primary hyperparathyroidism is the surgical removal of one or more of the parathyroid glands in the neck. There are currently no effective pharmaceutical therapies for the treatment of primary hyperparathyroidism. Studies suggest that over 30 percent of the estimated two million patients in the United States with chronic renal failure are affected by secondary hyperparathyroidism. Secondary hyperparathyroidism commonly develops during the early stages of chronic renal failure before dialysis is necessary. Approximately 85 percent of the estimated 300,000 acute renal failure patients who require either dialysis or renal transplant suffer from secondary hyperparathyroidism. Current treatment for secondary hyperparathyroidism includes calcium supplements, phosphate binding chemicals and vitamin D, none of which directly regulate the secretion of parathyroid hormone.

For more information:
drugs in development - cinacalcet HCl
therapeutic areas - hyperpararathyroidism

teduglutide

Approximately 25,000 adults and 7,000 children in North America are afflicted with short bowel syndrome. Many of these patients require total parenteral nutrition, the cost of which can exceed $100,000 annually per patient. There are currently no effective therapies available for enhancing the growth and repair of the cell lining of the small intestine. We believe that the short bowel syndrome market is an attractive one because of the high cost of treating patients and the absence of any effective drug therapies. We have been granted orphan drug designation for teduglutide for short bowel syndrome from the FDA, which provides, subject to several restrictions, seven years of marketing exclusivity once a product is approved for treatment of diseases that afflict fewer than 200,000 patients. The Commission of the European Communities has also recently designated teduglutide an orphan medicinal product for the treatment of short bowel syndrome.

We believe that teduglutide, if successful in the treatment of short bowel syndrome, may also be useful in treating other gastrointestinal conditions marked by inefficient absorption or altered absorptive capacity. Examples of these conditions include Crohn's disease, inflammatory bowel disease and intestinal mucositis in cancer patients. ■

For more information:
drugs in development - teduglutide
therapeutic areas - gastrointestinal disorders

NPS PHARMACEUTICALS

PREOS®

PREOS® is recombinantly produced, full-length human parathyroid hormone (PTH). The importance of calcium for healthy bones is well known. Less widely appreciated is the critical role PTH plays in the regulation of calcium physiology and bone replacement processes. It has now been well established that the normal daily rise and fall of PTH levels in the blood have a profound effect on bone, and that injections of PTH can stimulate the growth of structurally normal new bone in cases where bone has been lost to osteoporosis. In a Phase II clinical trial with over 200 postmenopausal women, daily injections of 100 micrograms of PREOS® produced a clinically and statistically significant average increase in bone mineral density of nearly 8% over the course of the study's one-year period.

PREOS® speeds up both bone formation and resorption with a resulting net increase in bone formation.

TOP Study

The pivotal Phase III clinical trial with PREOS® (termed the Treatment of Osteoporosis with PTH or TOP Study) is a double-blind, placebo-controlled, multi-center trial measuring increases in bone mineral density and PREOS's effectiveness in fracture reduction, to allow NPS to seek broad labeling for treating osteoporosis. The TOP Study, which concluded dosing in September 2003, was designed to evaluate the effects of PREOS® in postmenopausal women with low bone mineral density who may have suffered a fracture, but who were not receiving drug or hormone therapy for osteoporosis. Women participating in the study received daily, subcutaneous injections of PREOS® or placebo. Dosing in this study lasted for 18 months.

POWER Study

NPS is also conducting a clinical trial called the PTH for Osteoporotic Women on Estrogen Replacement, or POWER, Study. This study is being conducted at centers in Europe, which is the largest pharmaceutical market for osteoporosis outside the United States. Participants receive daily subcutaneous injections of PREOS® or placebo in addition to their ongoing hormone replacement therapy. Dosing in the trial is expected to last for 24 months.

PaTH Study

In addition, PREOS® is being tested in a clinical trial coordinated by the University of California, San Francisco and sponsored by the National Institutes of Health. This randomized, double-blind trial is referred to as the PTH

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and alendronate, or PaTH, Study. PREOS® and alendronate (Merck's Fosamax®) work in different ways.

PREOS® speeds up both bone formation and resorption with a resulting net increase in bone formation. Fosamax is an "anti-resorptive" drug that slows or halts the loss of bone due to resorption and is already approved by the Food and Drug Administration for the treatment of osteoporosis. The study includes approximately 240 women with low bone mineral density. Over a 24-month period, it will test whether PREOS® is more effective in building bone mineral density than Fosamax, and whether the combination of PREOS® and Fosamax® is more effective than either therapy alone. ■

Compassionate Use programs are not being considered at this time. If you have questions, please contact development and clinical studies.